Effects of oral cannabinoids on systemic inflammation and viral reservoir in people with HIV on antiretroviral therapy: results of the CTNPT 028 clinical trial

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BACKGROUND AND OBJECTIVES

Despite effective antiretroviral therapy (ART), people with HIV (PWH) continue to suffer from chronic systemic inflammation and persistent immune activation. This chronic inflammatory state can lead to early ageing and non-AIDS co-morbidities. In addition, heightened levels inflammation during ART is associated with the persistence of HIV reservoirs, the major obstacle to HIV eradication. Cannabinoids have demonstrated to exert anti-inflammatory properties *in vitro* and in SIV infected monkeys, but these anti-inflammatory properties had not yet been validated in a controlled clinical trial in the context of HIV. This study aimed to assess the effects of oral cannabinoids on systemic inflammation and the viral reservoir in PWH.

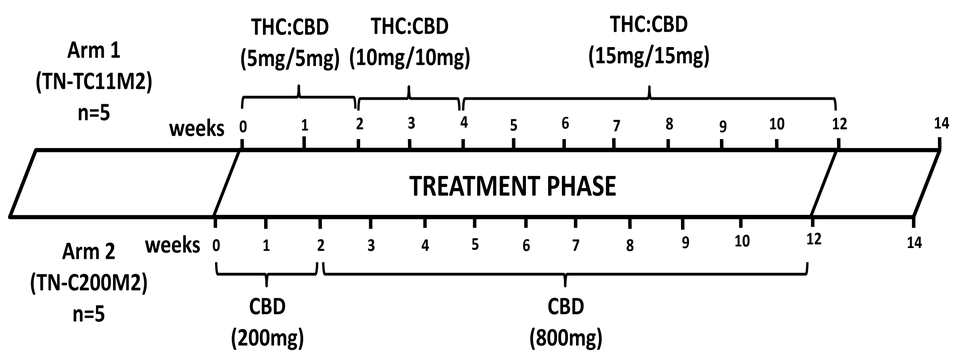
METHODS

- **Study design and population:** 10 PWH (median age: 57.5 years, 8 males) on ART were randomized (n=5/group) to **increasing doses of oral Δ9-tetrahydrocannabinol (THC): cannabidiol (CBD) combination (THC/CBD: 2.5/2.5 to 15/15mg daily; ARM 1) capsules or CBD-only (200 to 800mg daily; ARM 2)** capsules, for 12 weeks.
- **Schedule of visits and laboratory assays:**

Blood specimens were prospectively collected from each participant, 21 to 7 days prior to treatment initiation, at week 0 (at initiation of treatment), and weeks 1, 2, 6, 8, 12 (at treatment completion), and 14 (2 weeks after stopping the treatment).

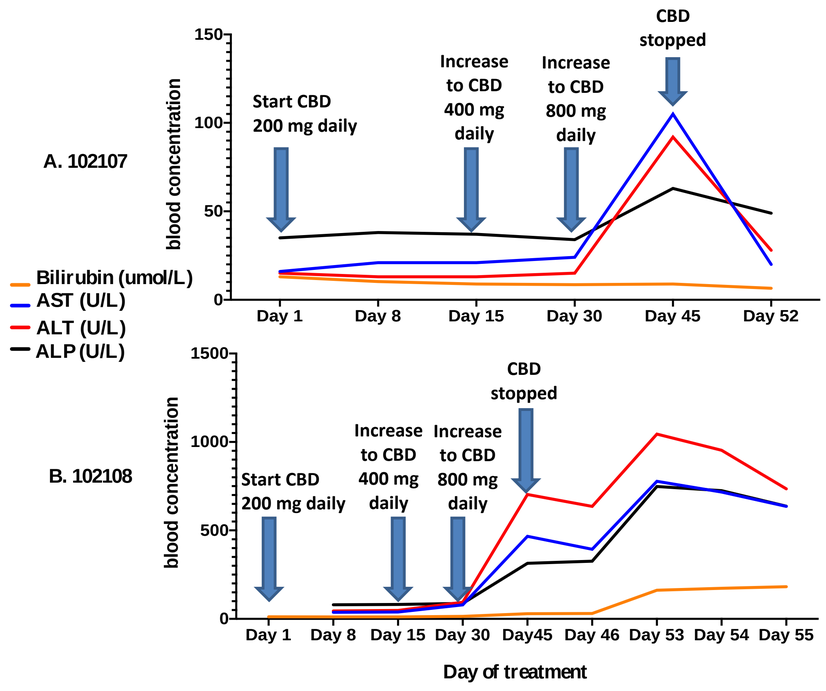
Plasma levels of inflammatory markers and cytokines were determined via Luminex and ELISA. T-cell and monocyte subsets were characterized by flow cytometry.

HIV-DNA and cell-associated HIV-RNA (LTR-gag) were measured in circulating CD4 T-cells by ultra-sensitive qPCR.

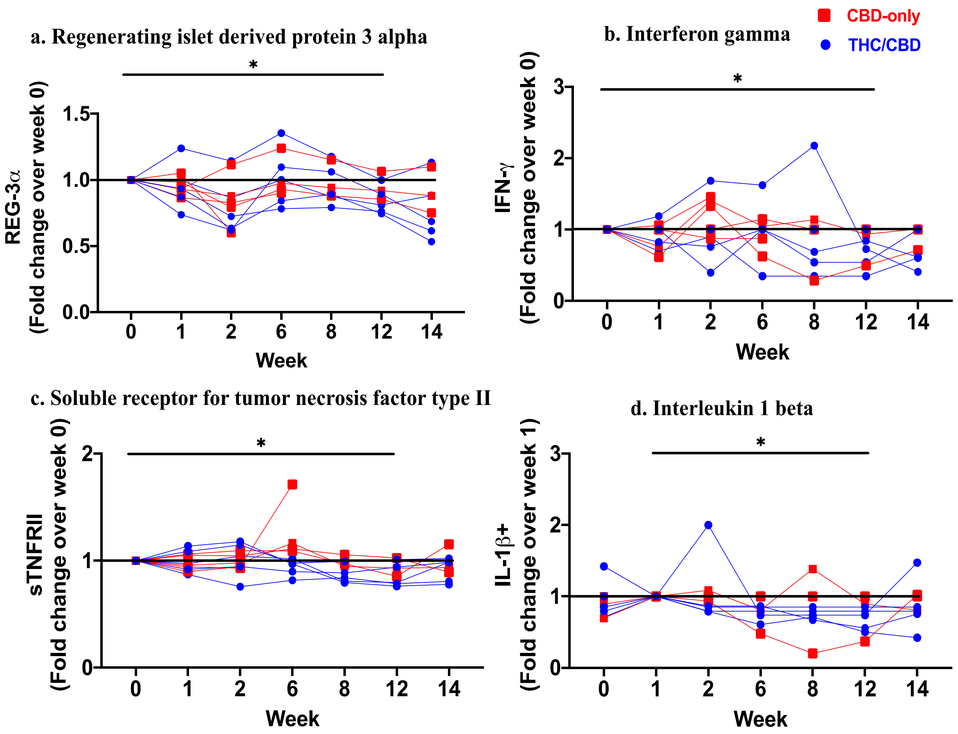


RESULTS

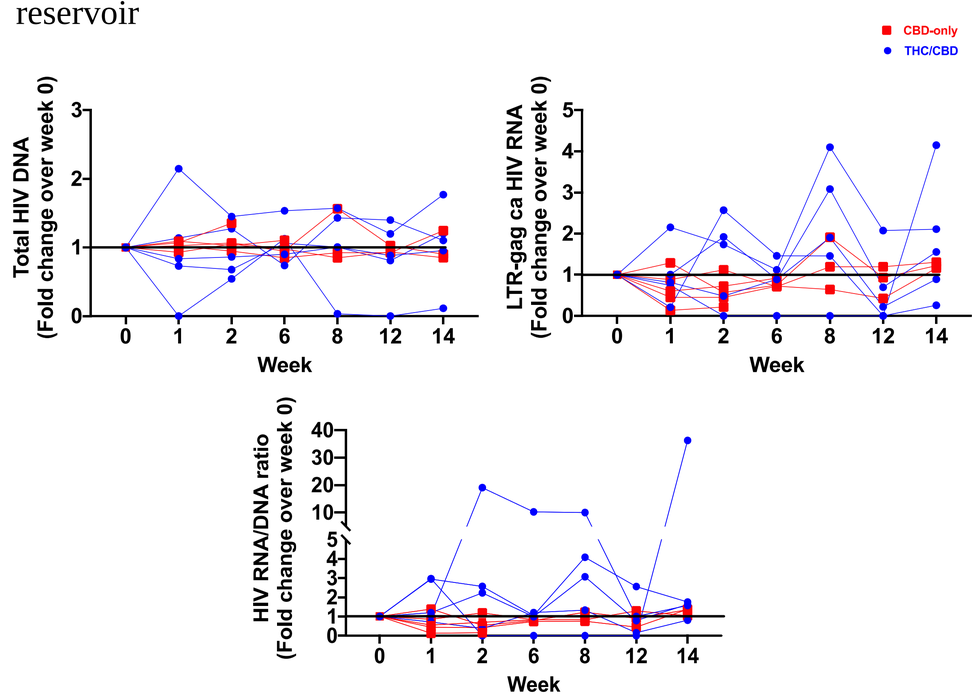
- Cannabinoids treatment did not affect hematology/biochemistry profiles of all the participants who completed the study (8/10);
- CD4 count and CD4/CD8 ratio were stable, and viral load remained suppressed over the treatment period for all the participants.
- Two participants who were withdrawn from the study showed transient elevation of liver enzymes.



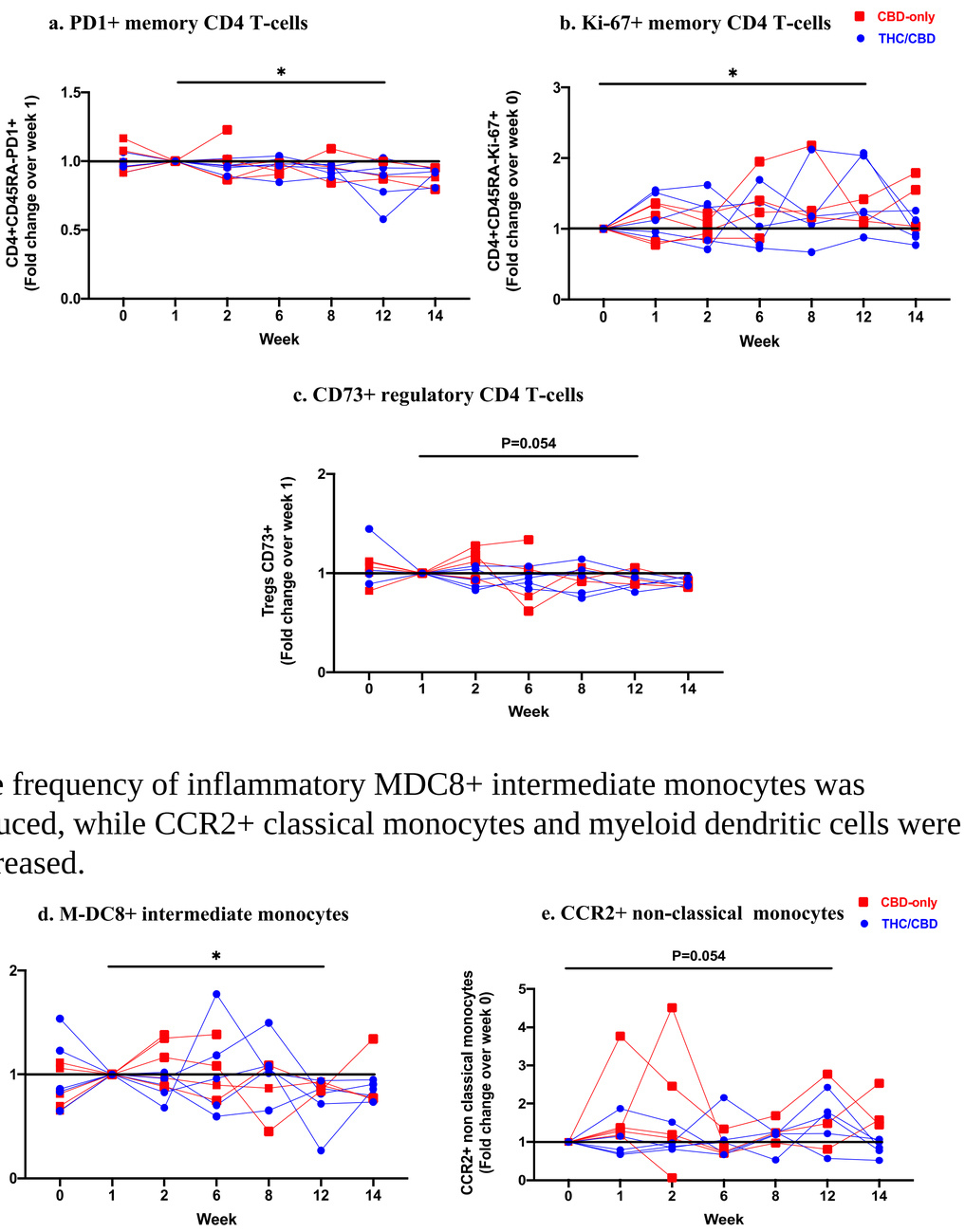
- Cannabinoids reduced soluble inflammatory markers in plasma



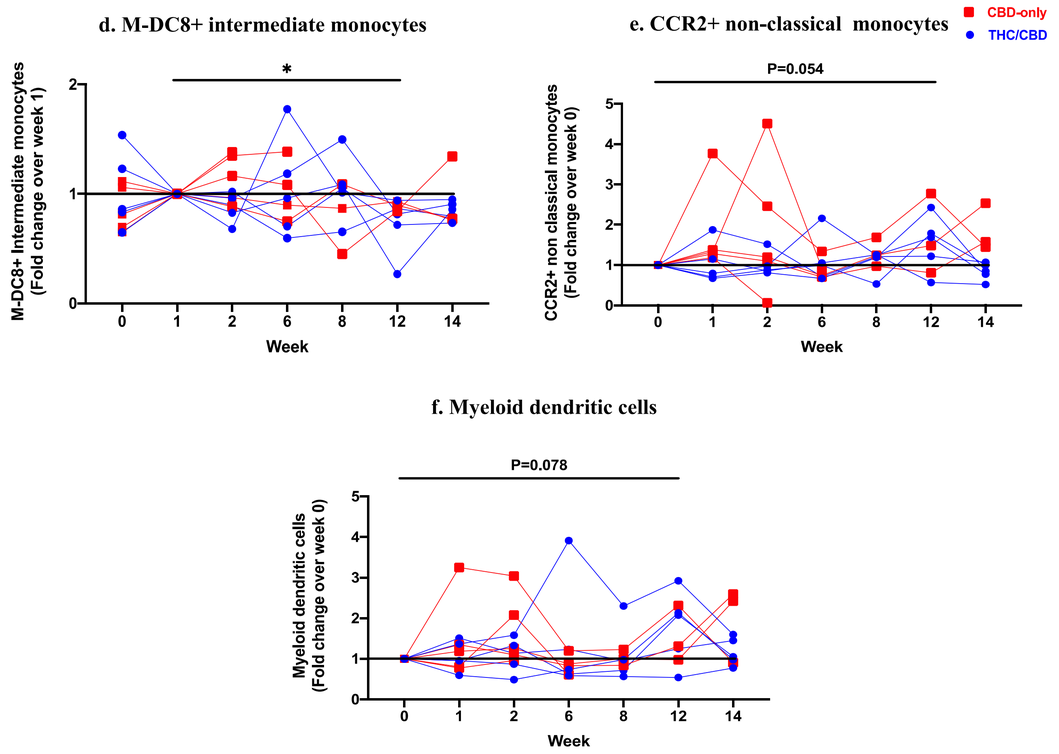
- No significant changes were observed in the dynamic of markers of HIV reservoir



- The frequencies of PD1+ memory, and CD73+ regulatory CD4 T-cells were reduced, while Ki-67+ memory CD4-T cells were increased.



- The frequency of inflammatory MDC8+ intermediate monocytes was reduced, while CCR2+ classical monocytes and myeloid dendritic cells were increased.



CONCLUSIONS

Oral cannabinoids could help reduce HIV-induced chronic inflammation. These findings can help guide future large clinical trials investigating anti-inflammatory properties of cannabinoids.

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